(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 November 2004 (04.11.2004)

PCT

(10) International Publication Number
WO 2004/093649 A2

(51) International Patent Classification[7]: A61B

(21) International Application Number: PCT/US2004/012065

(22) International Filing Date: 19 April 2004 (19.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/421,680 22 April 2003 (22.04.2003) US

(71) Applicant *(for all designated States except US)*: SUB-Q, INC. [US/US]; 1062-D Calle Negocio, San Clemente, CA 92673 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: ASHBY, Mark [US/US]; 23962 Frigate Drive, Laguna Niguel, CA 92677 (US). SING, Eduardo, Chi [US/US]; 5 Terraze Del Mar, Dana Point, CA 92629 (US).

(74) Agents: KREBS, Robert, E. et al.; Thelen Reid & Priest LLP, P.O. Box 640640, San Jose, CA 95164-0640 (US).

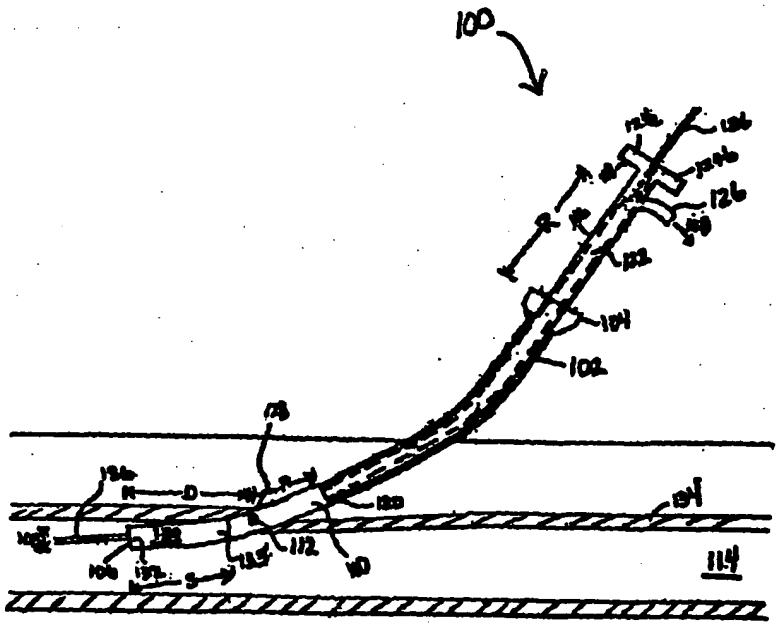
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

[Continued on next page]

(54) Title: PUNCTURE CLOSURE SYSTEME WITH PIN AND PULL TECHNIQUE



(57) Abstract: The present invention provides for a method and apparatus to facilitate hemostasis at a blood vessel puncture site having a cannula with a distal end, a proximal end, an inner diameter, and a lumen extending between said distal end and said proximal end; a bleed back port located near the distal end; a pusher having a top, a bottom, and a lumen extending between the top and bottom, the bottom is slidably received into the cannula lumen; a bleed back exit port located near the top; and a pledget having a first end and a second end, the first end positioned at the distal end within the cannula lumen, and the second end positioned below the bleed back port.

WO 2004/093649 A2

TITLE OF INVENTION

PUNCTURE CLOSURE SYSTEM WITH PIN AND PULL TECHNIQUE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of, and claims priority under 35 U.S.C. §120 to, and incorporates by reference herein in their entirety: 1. Co-pending application serial number 09/613,439, filed July 11, 2000, entitled "System And Method For Facilitating Hemostasis Of Blood Vessel Punctures With Absorbable Sponge" by inventors Andrew H. Cragg, Rodney Brenneman, and Mark Ashby which is a divisional of U.S. Patent No. 6,162,192, filed May 1, 1998; and 2. Co-pending application serial number 10/107,539, filed March 25, 2002, entitled "Apparatus And Method For Percutaneous Sealing Of Blood Vessel Punctures" by inventors Andrew H. Cragg, Rodney Brenneman, and Richard Greff, which is a divisional of U.S. Patent No. 6,371,974, filed August 2, 1999, which is a divisional of U.S. Patent No. 6,071,300, filed July 7, 1997, which is a continuation-in-part of U.S. Patent No. 5,645,566, filed September 15, 1995, by inventors Andrew H. Cragg, and Rodney Brenneman.

FIELD OF THE INVENTION

[0002] The present invention relates to facilitating hemostasis at a puncture site. More particularly, the present invention relates to facilitating hemostasis at a puncture site by delivering a hemostasis promoting material to the blood vessel puncture site using a pin and pull technique.

BACKGROUND OF THE INVENTION

[0003] A large number of diagnostic and interventional procedures involve the percutaneous introduction of instrumentation into a vein or artery. For example, coronary angioplasty, angiography, atherectomy, stenting of arteries, and many other procedures often involve accessing the vasculature through a catheter placed in the femoral artery or other blood vessel. Once the procedure is completed and the catheter or other instrumentation is removed, bleeding from the punctured artery must be controlled.

[0004] Traditionally, external pressure is applied to the skin entry site to stem bleeding from a puncture wound in a blood vessel. Pressure is continued until hemostasis has occurred at the puncture site. In some instances, pressure must be applied for up to an hour or more during which time the patient is uncomfortably immobilized. In addition, a risk of hematoma exists since bleeding from the vessel may continue beneath the skin until sufficient clotting effects hemostasis. Further, external pressure to close the vascular puncture site works best when the vessel is close to the skin surface but may be unsuitable for patients with substantial amounts of subcutaneous adipose tissue since the skin surface may be a considerable distance from the vascular puncture site.

[0005] There are several prior art devices that try to overcome the disadvantages of the traditional external pressure application. For example, there are devices that place a hemostat within the bloodstream of the vessel, within the wall of the blood vessel, or

adjacent to the wall of the blood vessel puncture site to close the puncture. However, reliance is on tactile sensation alone to indicate to the surgeon the proper placement of the puncture closing instrumentation. Other prior art references require a separate device for locating the blood vessel puncture site which is must then be removed for insertion of a second device to expel a hemostat. Still other prior art devices use bleed back ports to locate the blood vessel puncture site in conjunction with other devices such as a foot plate placed against the blood vessel wall or closure devices with anchors. However, in these prior art devices a surgeon is then required to use sutures and/or needles to close the blood vessel puncture. Moreover, in some of the prior art devices, external pressure applied at the surface of the skin may still be required.

[0006] Thus, there is still a need to perform the closing of a blood vessel puncture site with a more efficient and easier apparatus and method. There is a need for an apparatus and method to both accurately locate the blood vessel puncture site as well as facilitate hemostasis utilizing one instrument. Moreover, there is a need for a method and apparatus that can provide for the ex-vivo loading of a hemostat, provide for a more accurate location of the blood vessel puncture site, and is able to deliver a hemostat to the blood vessel puncture site all in a single pass. Furthermore, there is a need for an apparatus and method that can accurately deliver a hemostat in various positions that the surgeon desires or believes is best for the patient.

BRIEF DESCRIPTION OF THE INVENTION

[0007] The present invention provides for a method and apparatus to facilitate hemostasis at a blood vessel puncture site having a cannula with a distal end, a proximal end, an inner diameter, and a lumen extending between said distal end and said proximal end; a bleed back port located near the distal end; a pusher having a top, a bottom, and a lumen extending between the top and bottom, the bottom is slidably received into the cannula lumen; a bleed back exit port located near the top; and a pledget having a first end and a second end, the first end positioned at the distal end within the cannula lumen, and the second end positioned below the bleed back port.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] The accompanying drawings, which are incorporated into and constitute a part of this specification, illustrate one or more embodiments of the present invention and, together with the detailed description, serve to explain the principles and implementations of the invention.

In the drawings:

FIG. 1 illustrates an apparatus within a blood vessel lumen to facilitate hemostasis at a blood vessel puncture site in accordance with one embodiment of the present invention.

FIG. 2 illustrates an apparatus to facilitate hemostasis at a blood vessel puncture site in accordance with another embodiment of the present invention.

FIGS. 3A and 3B illustrates an apparatus to facilitate hemostasis at a blood vessel puncture site in accordance with yet another embodiment of the present invention.

FIGS. 4A-4H illustrates the various pledgets positioned within the blood vessel lumen.

FIGS. 5A-5B illustrates the pledget positioned within the blood vessel wall.

FIGS. 6A-6B illustrates the pledget positioned adjacent the blood vessel puncture site.

FIGS. 7A-7H illustrates a method for facilitating hemostasis at a blood vessel puncture site.

FIGS. 8A-8D illustrate embodiments of the pledget in accordance with the present invention.

DETAILED DESCRIPTION

[0009] Embodiments of the present invention are described herein in the context of a puncture closure system with pin and pull technique. Those of ordinary skill in the art will realize that the following detailed description of the present invention is illustrative only and is not intended to be in any way limiting. Other embodiments of the present invention will readily suggest themselves to such skilled persons having the benefit of this disclosure. Reference will now be made in detail to implementations of the present invention as illustrated in the accompanying drawings. The same reference indicators will be used throughout the drawings and the following detailed description to refer to the same or like parts.

[0010] In the interest of clarity, not all of the routine features of the implementations described herein are shown and described. It will, of course, be appreciated that in the development of any such actual implementation, numerous implementation-specific decisions must be made in order to achieve the developer's specific goals, such as compliance with application- and business-related constraints, and that these specific goals will vary from one implementation to another and from one developer to another. Moreover, it will be appreciated that such a development effort might be complex and time-consuming, but would nevertheless be a routine undertaking of engineering for those of ordinary skill in the art having the benefit of this disclosure.

[0011] Referring now to Fig. 1, an embodiment of the present invention illustrating an apparatus within a blood vessel lumen to facilitate hemostasis at a blood vessel puncture

site. The apparatus 100, comprises a delivery cannula 102 having a distal end 106, a proximal end 104, an inner diameter 108, and a lumen 110 extending between the distal end 106 and the proximal end 104. The cannula 102 may also have a bleed back port 112 located near the distal end 106 of the cannula 102 to detect blood flow out of the blood vessel lumen. The present invention allows for the synergistic coexistence of both a hemostatic agent and a bleed back system. Both do not compete or detract from each of their functions which allows a user to locate the blood vessel puncture site using visual bleed back indication and to deploy a hemostatic agent to the blood vessel puncture site in one single pass.

[0012] The apparatus 100 may have a pusher 116 with a top 118, a bottom 120, and a lumen 122 extending between the top 118 and bottom 120. The pusher bottom 120 may be placed inside the cannula lumen 110 such that the pusher 116 may be able to slidably move within the cannula lumen 110. The pusher bottom 120 may have a diameter equal to or less than the inner diameter of the cannula 108. The diameter may be as small as 1 French, but preferably greater than 3 French. Moreover, it is preferable that the pusher bottom 120 have a diameter substantially equal to the inner diameter of the cannula 108 to maximize visual bleed back indication as further discussed below. The pusher top 118 may have a pair of finger levers 124a and 124b to assist a user in holding the pusher 116 in a fixed position or to assist in moving the pusher 116 within the cannula lumen 110. However, those of ordinary skill in the art will now realize that any other means for grasping or holding the pusher 116 may be used.

[0013] The pusher 116 may also have a bleed back exit port 126 located near the pusher top 118. Blood flow entering the apparatus 100 from the bleed back port 112 will flow through the pusher lumen 122 and out the bleed back exit port 126 as indicated by arrow 128. Alternatively, as shown in Fig. 2, another embodiment of the present invention illustrating an apparatus to facilitate hemostasis at a blood vessel puncture site, the bleed back exit port 202 may be located near the cannula proximal end 104. In this case, blood will flow from the bleed back port 112, through the cannula lumen 110, and out the bleed back exit port 202 as indicated by arrow 204.

[0014] When the bleed back port 112 is located within the blood vessel lumen 114, a steady stream of blood will flow out of the bleed back exit port 126. However, when the bleed back port is positioned outside the blood vessel lumen (not shown) or within the wall of the blood vessel, blood will not steadily flow out of the bleed back exit port 126. This visual indication of blood flow out of the bleed back exit port 126, 202 assists a user in positioning the apparatus 100 at the blood vessel puncture site 128.

[0015] To maximize the visual effects of bleed back, it is preferable that the lumen 110 and the plunger lumen 122, through which the blood flows to the bleed back exit port 126, 202 be maximized. The present invention allows for an accurate visual bleed back indication by maximizing the lumen 110 through the use of a cannula 102. To further provide accurate visual bleed back indication it is preferable that the pusher lumen 122 be substantially equal or between about 0.5 French to 0.2 French smaller than the inner diameter of the cannula 108 as shown in Fig. 1. Alternatively, a shown in Fig. 2, it is

preferable that obstructions within the cannula lumen 110 be eliminated and the pusher bottom 120 be positioned above the bleed back exit port 202.

[0016] In an alternative embodiment, as shown in Figs. 3A and 3B, the pusher 302 may be a stylet and disk or any other similar type of pusher 312. In these embodiments, the bleed back exit port 304 is located near the cannula proximal end 104. The pusher 302 may have a disk or piston 306, a top 308, and an extension 310 between the disk 306 and the top 308. As shown in Figs. 3A and 3B, the stylet may be attached to the disk as a single unit, may be attached to the disk by other means such as a string 314, or the stylet and disk may not be attached together. The disk 306 may be located below the bleed back port 112 adjacent the pledget second end 133. The disk 306 may have a diameter substantially equal to the inner diameter of the cannula 108, but it may be smaller than the inner diameter of the cannula 108. It is preferable that the diameter of the extension or stylet 310 be as small as possible, for example less than 3 French, yet be strong enough to eject the pledget 130 from the cannula 102. This allows for maximum space within the cannula lumen 110 for blood to flow from the bleed back port 112 to the bleed back exit port 304. Moreover, the stylet may be configured in any shape such as a shaft as shown in Figs. 3A and 3B or as a plenum (not shown) to divide the cannula lumen into two or more lumens.

[0017] The apparatus 100 may also have a pledget 130 compressed within the cannula lumen 110 at the cannula distal end 106. The pledget 130 is positioned below the bleed back port 112 such that the pledget serves as the distal "seal" or the boundary of the

bleed back circuit. The pledget 130 may be any biocompatible material, preferably a sponge. Preferably, the sponge is non-immunogenic and may be absorbable, dissolved or resorbed by the body, or non-absorbable. Non-absorbable pledgets may include various polymeric foams, such as polyurethanes, as are well-known in the art. Absorbable sponges may include those made from Gelatin, Colagen, Oxydized Cellulose, PGA, and other like materials.

[0018] The pledget 130 may also have a coagulant or clot formation accelerating agent such as Thrombin, Fibrinogen (Biomolecules), Protamine, and additives that can create a negative or positive charged pledget such as calcium chloride, magnesium, ferric chloride, or an acid such as hydrochloric acid, and other similar additives. The coagulants are used to effect local hemostasis and chemically activate a clotting cascade. The coagulants may be incorporated into the pledget as part of the gelatin formation or may be applied as a coating to the surface of a pledget.

[0019] The pledget 130 may be pre-hydrated to facilitate rapid expansion or the pledget 130 may contain a wetting agent for rapid expansion of the pledget with or without pre-hydrating the pledget. The pledget 130 may be pre-hydrated in various ways as disclosed in detail in U.S. Patent No. 6,071,301, filed May 1, 1998, entitled "Device And Method For Facilitating Hemostasis Of A Biopsy Tract" by inventors Andrew H. Cragg, Rodney Brenneman, and Mark Ashby and U.S. Patent No. 6,162,192, filed May 1, 1998, entitled "System And Method For Facilitating Hemostasis Of Blood Vessel Punctures With Absorbable Sponge" by inventors Andrew H. Cragg, Rodney Brenneman, and Mark

Ashby both of which are hereby incorporated by reference in their entirety. Wetting agents are discussed in detail in co-pending application serial number 10/068,812, filed February 4, 2002, entitled "Cross-Linked Gelatin Composition Comprising A Wetting Agent" by inventor Richard J. Greff which is hereby incorporated by reference in its entirety. The wetting agents may be incorporated into the pledget as part of the gelatin formation or may be applied as a coating to the surface of a pledget.

[0020] The pledget 130 may also comprise a surface coating made of bioadhesive agents to increase surface traction and/or adhesion which will increase grip and friction between the surrounding tissue or artery wall and pledget. This will ensure that the pledget remains within the lumen of the blood vessel, intraarteriotomy the blood vessel wall, or within the tissue tract adjacent the blood vessel puncture site. The bioadhesive agent may be a permanent tissue adhesive and/or bonding agent such as cyanoacrylates or fibrin derived compositions. Alternatively, the bioadhesive agent may be mucoadhesives that are triggered by moisture such as blood. Some synthetic mucoadhesives are polyvinyl carboxylic acids such as polyacrylic and methacrylic acids. Examples of such acids are Carbopol-974 NF (high performance polymer) and Noveon-AA1 sold by Noveon, Inc. located in Cleveland, Ohio. Additionally, cellulosics and polysaccarides may be used such as Poly(methyl vinyl ether - alt - Melaic Anhydride), Carboxymethyl Cellulose (sodium salt), and Chitosan (high molecular weight) sold by Aldrich Chemical Company, Inc. located in Milwauikee, WI. The bioadhesive agents may be incorporated

into the pledget as part of the gelatin formation or may be applied as a coating to the surface of a pledget.

[0021] As shown in Figs. 4B-4E, the pledget 130 may comprise a securing mechanism at the pledget first end 132 to secure the pledget to the blood vessel lumen 114, the intraarteriotomy the blood vessel wall, or provide friction and/or traction to the blood vessel wall. Alternatively, the securing mechanism may be located proximally of the pledget first end 132 along the pledget length, including at the pledget second end 133, to secure the deployed pledget against any movement. As shown in Fig. 4B, the securing mechanism may be a pair of lateral projections 400a, 400b or more centrally originating star configuration 402, or a retention flange 410 or proximal shoulders 413 on the outer surface of a distal dissolvable tip 412 as shown in Figs. 4G and 4H. Other proximally located pledget securing mechanisms may be used such as the expandable clip 800 shown in Fig. 8A, the proximal shuttlecock 802 shown in Fig. 8B, the expandable pineapple 804 shown in Fig. 8C, a trampoleen or umbrella frame 806 as shown in Fig. 8D, or other gripping features such as a crisscross surface, expandable braid, ridges, or bumps to prevent proximal movement after the pledget is deployed. All of these securing mechanisms can be retained within the cannula lumen in a non-deployed position (not shown) and upon deployment from the cannula, the securing features activate as shown in Figs. 8A-D. As shown in Fig. 4C, illustrating a pledget in a non-deployed state, the lateral projections 400a, 400b may be retained within the cannula lumen 110 at the cannula distal end 106 prior to deployment. After the pledget 130 is deployed, the lateral projections 400a, 400b expand as shown in Fig. 4D. The lateral projections may be made

of any biocompatible material such as various polymers that are well known in the art. The lateral projections may also be made of non-absorbable materials such as SST, nitinol, titanium, or other biocompatible metals. The projections may also be made of absorbable polymers such as PGA, Gelatin, methyl cellulose, carboxymethyl cellulose, carbowaxes, and gelatin (particularly pigskin gelatin). Among the suitable polymers are polylactic glycolic acids, polyvinyl pyrrolidone, polyvinyl alcohol, polyproline, and polyethylene oxide.

[0022] In yet another embodiment, the pledget first end 132 may extend partially out of the cannula distal end 106 as shown in Fig. 4F. Thus, the pledget first end 132 will have a diameter equal to the outside diameter of the cannula 404.

[0023] Additionally, the pledget first end 132 may have different characteristics than the pledget second end 133. For example, the first end 132 may vary in traction, stickiness, hardness, dissolution rate, thrombocinicity, shape, or other similar characteristics from the second end 133.

[0024] As shown in Fig. 1, the pledget 130 may have a first end 132 and a second end 133 where the first end 132 may be positioned immediate the cannula distal end 106. It is preferable that the diameter of the pledget first end 132 be substantially equal to the inner diameter of the cannula 102 to prevent blood from flowing though the cannula distal end 106. The second end 133 may be positioned below the bleed back port 112. The pledget

130 may expand when exposed to fluids such as blood or when expelled out of the cannula lumen 110.

[0025] The embodiments above may be used with or without a guidewire 136 or other locating device. If used with a guidewire 136, the entire pledget 130 may have an axial passage (not shown) through its length, S, to receive a guidewire or the like. If used without a guidewire, the present invention may be placed within an existing procedural sheath already positioned within the artery or blood vessel (not shown). However, if a procedural sheath is used, the bleed back port 112 must extend beyond the procedural sheath distal end such that bleed back may be detected to properly position the apparatus 100.

[0026] To locate the apparatus 100 in the proper position, the user may insert the apparatus 100 down the tissue tract until the bleed back port 112 enters the blood vessel lumen 114 as indicated by when bleeding is first observed exiting the bleed back exit port 126. The user may then withdraw the apparatus 100 out of the blood vessel lumen 114 until the bleed back port 126 is located within the wall of the blood vessel 134 as indicated by when bleeding is no longer observed exiting the bleed back exit port 126.

[0027] After the apparatus 100 is positioned in the proper position at the blood vessel puncture site 128 as shown in Fig. 1, the pledget 130 may be positioned in several positions to facilitate hemostasis at the blood vessel puncture site 128. One position may be within the blood vessel lumen, as shown in Figs. 4a and 4b. Another position may be

within the blood vessel wall or intraarteriotomy 500 as shown in Figs. 5a and 5b. Still another position may be adjacent the wall of the blood vessel 134 as shown in Fig. 6.

[0028] To position the pledget 130 within the blood vessel lumen 114 as shown in Figs. 4a and 4b, distance D (Fig. 1), the distance between the cannula distal end 106 and the bleed back port 112, may be greater than or equal to distance S, the length of the pledget 130. Moreover, distance S may be greater than distance P, the distance between the bleed back port 112 and the pusher bottom 120. With the pusher 116 in a fixed or pinned positioned, the cannula 102 may be pulled back a distance R such that the cannula proximal end 104 is adjacent the pusher top 118. Distance R may be greater than or equal to the sum of distances D and P. The pledget first end 132 is positioned approximately a distance S-P within the blood vessel lumen 114.

[0029] When using a pledget 130 with a securing mechanism at the pledget first end 132, the cannula 102 may be pulled back a distance R or in the alternative, the cannula 102 may be fixed and pusher 116 pushed down a distance R where R is described by:

$$\text{Minimum distance to expose the securing mechanism} \leq R \leq D+P \quad (1)$$

Distance R may be less than the sum of distances D and P such that only the securing mechanism is exposed beyond the cannula distal end 106 when the cannula 102 is pulled back a distance R or the pusher 116 is pushed down distance R as shown in FIG. 7D. In this position, the securing mechanism is exposed within the blood vessel lumen 704 and expands. The cannula 102 and pusher 116 may then be simultaneously pulled out of the tissue tract such that the securing mechanism catches the inside wall of the blood vessel

134 which secures the pledget 130 at the blood vessel puncture site 128 to facilitate hemostasis.

[0030] To position the pledget 130 within the wall of the blood vessel as shown in Figs. 5a and 5b, the distance D (Fig. 1), the distance between the cannula distal end 106 and the bleed back port 112, may be greater than or equal to distance S, the length of the pledget 130. Moreover, distance S is equal to distance P, the distance between the bleed back port 112 and the pusher bottom 120. With the pusher 116 in a fixed or pinned positioned, the cannula 102 may be pulled back a distance R such that the cannula proximal end 104 is adjacent the pusher top 118. Distance R may be greater than or equal to the sum of distances D and P.

[0031] As shown in Fig. 7D, when using a pledget 130 with a securing mechanism at the pledget first end 132, the cannula 102 may be pulled back a distance R or in the alternative, the cannula 102 may be fixed and pusher 116 pushed down a distance R, where R is described as follows:

[0032] Minimum distance to expose the securing mechanism $\leq R \leq D+P$ (2)

Distance R may be less than the sum of distances D and P such that only the securing mechanism is exposed beyond the cannula distal end 106 when the cannula 102 is pulled back a distance R or the pusher 116 is pushed down distance R. In this position, the securing mechanism is exposed within the blood vessel lumen 704 and expands. The cannula 102 and pusher 116 may then be simultaneously pulled out of the tissue tract

such that the securing mechanism catches the inside wall of the blood vessel 134 which secures the pledget 130 at the blood vessel puncture site 128 to facilitate hemostasis.

[0033] To position the pledget 130 adjacent the blood vessel puncture site 128 as shown in Fig. 6A, distance D (Fig. 1), the distance between the cannula distal end 106 and the bleed back port 112, may be greater than or equal to distance S, the length of the pledget 130. Moreover, distance S may be less than distance P, the distance between the bleed back port 112 and the pusher bottom 120. With the pusher 116 in a fixed or pinned positioned, the cannula 102 may be pulled back a distance R such that the cannula proximal end 104 is adjacent the pusher top 118. Distance R may be greater than or equal to the sum of distances D and P. The pledget first end 132 is positioned approximately a distance P-S outside the blood vessel puncture site 128. As illustrated in Fig. 6B, a pledget with distally extending lateral prongs 600a and 600b may also be used to effectively place the pledget 130 adjacent the blood vessel puncture site 128.

[0034] When using the embodiments in Fig. 2 or Fig. 3, once the apparatus 100 is properly positioned at the blood vessel puncture site 128, the pusher bottom 306 is then positioned at distance P prior to deployment of the pledget 130. The distance P may vary depending on whether the pledget 130 is deployed within the blood vessel lumen, within the blood vessel wall, or adjacent the blood vessel puncture site.

[0035] Figs. 7A-7H illustrates a method for facilitating hemostasis at a blood vessel puncture site. As shown in Fig. 7A, a cannula 700 has a bleed back port 706 at the

cannula distal end 708 and a pledget 710 positioned below the bleed back port 706. The cannula 700 and pusher 702 are advanced into the blood vessel lumen 704 until the bleed back port 706 is located within the blood vessel lumen 704. In this position, blood flows into the bleed back port 706, through the pusher lumen 712, and out a bleed back exit port 714 as indicated by arrow 724. When the bleed back port 706 is located within the blood vessel lumen 704, a steady stream of blood will flow out of the bleed back exit port 714. However, when the bleed back port is positioned outside the blood vessel lumen or within the wall of the blood vessel as further discussed below in Fig. 7B, blood will not steadily flow out of the bleed back exit port 714. This visual indication of blood flow out of the bleed back exit port 714 assists a user in positioning the apparatus 716 at the blood vessel puncture site 718.

[0036] The apparatus may be used with or without a guidewire 722 or other locating device. If used with a guidewire 722, the pledget 710 may have an axial passage (not shown) through its length to receive a guidewire or the like. If used without a guidewire, the present invention may be placed within an existing procedural sheath already positioned within the artery or blood vessel (not shown). However, if a procedural sheath is used, the bleed back port 706 must extend beyond the procedural sheath distal end such that bleed back may be detected to properly position the apparatus 716.

[0037] Alternatively, the bleed back exit port 202 may be located near the cannula proximal end as shown in Fig. 2. In this embodiment, blood will flow from the bleed back port 112, through the cannula lumen 110, and out the bleed back exit port 202. It is

preferable that the cannula lumen 110 have little to no obstructions to maximize blood flow through the lumen to the bleed back exit port 202 to provide an accurate visualization of bleed back. Thus, it is preferred that the pusher bottom 120 be positioned above the bleed back exit port 202. Alternatively, as shown in Figs. 3A and 3B, the pusher 302 may be a stylet and disk or any other similar type of pusher 312. As illustrated in Figs. 3A and 3B, the stylet may be attached to the disk as a single unit, may be attached to the disk by other means such as a string 314, or the stylet and disk may not be attached. The disk 306 may be located below the bleed back port 112 adjacent the pledget second end 133. The disk 306 may have a diameter equal to or less than the inner diameter of the cannula. The disk diameter may be as small as 1 French, but preferably greater than 3 French. It is also preferable that the diameter of the stylet or extension 310 be as small as possible, such as less than 3 French, yet be strong enough to eject the pledget from the cannula. This allows for maximum space within the cannula lumen 110 for blood to flow from the bleed back port 112 to the bleed back exit port 304. Moreover, the stylet may be configured in any shape such as a shaft as shown in Figs. 3A and 3B or as a plenum (not shown) to divide the cannula lumen into two or more lumens.

[0038] Fig. 7B shows the apparatus later in time than Fig. 7A. The cannula 700, pledget 710, bleed back port 706, and pusher 702 are simultaneously withdrawn from the blood vessel lumen 704 until bleed back is no longer visible out of the bleed back exit port 714. This informs a user that the apparatus 716 is located at or near the blood vessel puncture site 718.

[0039] The pledget 710 may be discharged to facilitate hemostasis once the apparatus is positioned at the proper position. When using embodiments of Figs. 2 and 3, the pusher 116 may be repositioned at distance P prior to deployment of the pledget 130. The distance P may vary depending on whether the pledget 710 is deployed within the blood vessel lumen, within the blood vessel wall, or adjacent the blood vessel puncture site as further discussed below.

[0040] The pledget 710 may be positioned in several positions to facilitate hemostasis at the blood vessel puncture site 718. One position is within the blood vessel lumen 704 as shown in Figs. 7C – 7E. Another position is within the blood vessel wall or intraarteriotomy 742 as shown in Figs. 7F and 7G. Still another position is adjacent the wall of the blood vessel 718 as shown in Fig. 7H.

[0041] To position the pledget 710 within the blood vessel lumen 704 as shown in Figs. 7C-7E, distance D (Fig. 7B), the distance between the cannula distal end 708 and the bleed back port 706, may be greater than or equal to distance S, the length of the pledget 710. Moreover, distance S may be greater than distance P, the distance between the bleed back port 706 and the pusher bottom 726. As shown in Fig, 7C, with the pusher 702 in a fixed or pinned positioned, the cannula 700 may be pulled back a distance R in the direction of arrow 732 such that the cannula proximal end 728 is adjacent the pusher top 730. Distance R may be greater than or equal to the sum of distances D and P. The pledget first end 734 is positioned approximately a distance S-P within the blood vessel lumen 704.

[0042] In another embodiment as shown in Figs. 7D and 7E, a pledget with a securing mechanism may be used. The securing mechanism may be located at the pledget first end, the pledget second end, or along the pledget length to secure the deployed pledget against any movement. The securing mechanism may be a pair of lateral projections as shown in Figs. 7D and 7E, an expandable clip 800 shown in Fig. 8A, the proximal shuttlecock 802 shown in Fig. 8B, the expandable pineapple 804 shown in Fig. 8C, a trampoleen or umbrella frame 806 as shown in Fig. 8D, or other gripping features such as a crisscross surface, expandable braid, ridges, or bumps.

[0043] When using a pledget 710 with a securing mechanism 736 at the pledget first end 734, it is compressed in its non-deployed state within the cannula lumen. With the pusher 702 fixed, the cannula 700 may be pulled back a distance R or in the alternative, cannula 700 may be fixed and pusher 702 pushed down the cannula a distance R. Distance R may be less than the sum of distances D and P and equal to or greater than the length of the securing mechanism 736. Distance R is the a length such that the securing mechanism 736 is exposed beyond the cannula distal end 708 when the cannula 700 is pulled back or, in the alternative, the pusher 702 is advanced down the cannula a distance R. In this position, as shown in Fig. 7D, the securing mechanism 736 is exposed within the blood vessel lumen 704 and expands. A portion or all of the pledget second end remains inside the cannula 700. As shown in Fig. 7E, the cannula 700 and pusher 702 may then be simultaneously pulled out of the tissue tract in the direction of arrow 732 such that the securing mechanism catches the inside wall of the blood vessel 740 which

secures the pledget 710 at the blood vessel puncture site 718 to remove the pledget 710 from the cannula 700 and facilitate hemostasis.

[0044] To position the pledget 710 within the blood vessel wall as shown in Figs. 7F and 7G, the distance D (Fig. 7B), the distance between the cannula distal end 708 and the bleed back port 706, may be greater than or equal to distance S, the length of the pledget 710. Moreover, distance S is equal to distance P, the distance between the bleed back port 716 and the pusher bottom 726. As shown in Fig. 7F, with the pusher 702 in a fixed or pinned positioned, the cannula 700 may be pulled back a distance R in the direction of arrow 732 such that the cannula proximal end 728 is adjacent the pusher top 730. Distance R may be greater than or equal to the sum of distances D and P.

[0045] In another embodiment, as shown in Figs. 7G which is similar to Fig. 7D, when using a pledget 710 with a securing mechanism 736 at the pledget first end 734, the securing mechanism 736 it is compressed in its non-deployed state within the cannula lumen. With the pusher fixed, the cannula 700 may be pulled back a distance R or in the alternative, cannula 700 may be fixed and pusher 702 pushed down the cannula a distance R. Distance R may be less than the sum of distances D and P and equal to or greater than the length of the securing mechanism 736. Distance R is the a length such that only the securing mechanism 736 is exposed beyond the cannula distal end 708 when the cannula 700 is pulled back or, in the alternative, the pusher 702 is advanced down the cannula a distance R. In this position, as shown in Fig. 7D, the securing mechanism 736 is exposed within the blood vessel lumen 704 and expands. A portion or all of the

pledget second end remains inside the cannula 700. As shown in Fig. 7E, the cannula 700 and pusher 702 may then be simultaneously pulled out of the tissue tract in the direction of arrow 732 such that the securing mechanism catches the inside wall of the blood vessel 740 which secures the pledget 710 at the blood vessel puncture site 718 to remove the pledget from the cannula and to facilitate hemostasis.

[0046] To position the pledget 710 adjacent blood vessel puncture site 718 as shown in Fig. 7H, distance D (Fig. 7B), the distance between the cannula distal end 708 and the bleed back port 706, may be greater than or equal to distance S, the length of the pledget 710. Moreover, distance S may be less than distance P, the distance between the bleed back port 706 and the pusher bottom 726. As shown in Fig. 7H, with the pusher 702 in a fixed or pinned positioned, the cannula 700 may be pulled back a distance R in the direction of arrow 732 such that the cannula proximal end 728 is adjacent the pusher top 730. Distance R may be greater than or equal to the sum of distances D and P. The pledget first end 734 is positioned approximately a distance P-S outside the blood vessel puncture site 718.

[0047] While embodiments and applications of this invention have been shown and described, it would be apparent to those skilled in the art having the benefit of this disclosure that many more modifications than mentioned above are possible without departing from the inventive concepts herein. The invention, therefore, is not to be restricted except in the spirit of the appended claims.

CLAIMS

What is claimed is:

1. An apparatus to facilitate hemostasis at a blood vessel puncture site, comprising:

a cannula having a distal end, a proximal end, an inner diameter, and a lumen extending between said distal end and said proximal end;

a bleed back port located near said distal end;

a pusher having a top, a bottom, and a lumen extending between said top and said bottom, said bottom to be slidably received into said cannula lumen;

a bleed back exit port located near said top;

a pledget having a first end and a second end, said first end positioned at said distal end within said cannula lumen, said second end positioned below said bleed back port.

2. The apparatus of claim 1 further comprising a guidewire slidably received into said pusher lumen, said cannula lumen, said pledget, and said blood vessel puncture site.

3. The apparatus of claim 1 wherein said pusher bottom has a diameter substantially equal to or less than the inner diameter of said cannula.

4. The apparatus of claim 1 further comprising:

a first distance between said proximal end and said top;

a second distance between said bleed back port and said bottom;

a third distance between said distal end and said bleed back port; and

a fourth distance between said first end and said second end.

5. The apparatus of claim 4 wherein said third distance is greater than or equal to said fourth distance and said first distance is greater or equal to a combination of said second and third distance.

6. The apparatus of claim 5 wherein said fourth distance is greater than said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent to said pusher top, said pledget first end is positioned within a wall of said blood vessel.

7. The apparatus of claim 5 wherein said fourth distance is less than said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent said pusher top, said pledget first end is positioned within a lumen of said blood vessel.

8. The apparatus of claim 5 wherein said fourth distance is equal to said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent to said pusher top, said pledget first end is positioned adjacent said blood vessel puncture site.

9. The apparatus of claim 1 wherein said pledget first end has a diameter substantially equal to the inner diameter of said cannula.

10. The apparatus of claim 1 wherein said pledget further comprises a hemostatic agent to chemically activate a clotting cascade.

11. The apparatus of claim 1 wherein said pledget further comprises a wetting agent.

12. The apparatus of claim 1 wherein said pledget further comprises a securing mechanism.

13. The apparatus of claim 12 wherein said securing mechanism is a bioadhesive agent.

14. The apparatus of claim 12 wherein said securing mechanism is coupled to said pledget first end.

15. The apparatus of claim 12 wherein said securing mechanism is coupled to said pledget second end.

16. The apparatus of claim 12 wherein said securing mechanism comprises at least one expandable prong.

17. The apparatus of claim 12 wherein said securing mechanism comprises at least one lateral projection.

18. The apparatus of claim 12 wherein said securing mechanism is expandable.

19. The apparatus of claim 12 wherein said securing mechanism is absorbable.

20. An apparatus to facilitate hemostasis at a blood vessel puncture site, comprising:

a cannula having a distal end, a proximal end, an inner diameter, and a lumen extending between said distal end and said proximal end;

a bleed back port located near said distal end;

a bleed back exit port located near said proximal end;

a pusher having a top and a bottom, said bottom to be slidably received into said cannula lumen;

a pledget having a first end and a second end, said first end positioned at said distal end within said cannula lumen, said second end positioned below said bleed back port.

21. The apparatus of claim 20 wherein said pusher bottom has a diameter equal to or less than the inner diameter of said cannula.

22. The apparatus of claim 20 further comprising:

a first distance between said proximal end and said top;

a second distance between said bleed back port and said bottom;

a third distance between said distal end and said bleed back port; and

a fourth distance between said first end and said second end.

23. The apparatus of claim 22 wherein said third distance is greater than or equal to said fourth distance and said first distance is greater than or equal to a combination of said second and third distance.

24. The apparatus of claim 23 wherein said fourth distance is greater than said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent to said pusher top, said pledget first end is positioned within a wall of said blood vessel.

25. The apparatus of claim 23 wherein said fourth distance is less than said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent said pusher top, said pledget first end is positioned within a lumen of said blood vessel.

26. The apparatus of claim 23 wherein said fourth distance is equal to said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent to said pusher top, said pledget first end is positioned adjacent said blood vessel puncture site.

27. The apparatus of claim 20 wherein said pledget first end has a diameter substantially equal to the inner diameter of said cannula.

28. The apparatus of claim 20 wherein said pledget further comprises a wetting agent.

29. The apparatus of claim 20 wherein said pledget further comprises a securing mechanism.

30. The apparatus of claim 29 wherein said securing mechanism is a bioadhesive agent.

31. The apparatus of claim 29 wherein said securing mechanism is coupled to said pledget first end.

32. The apparatus of claim 29 wherein said securing mechanism is coupled to said pledget second end.

33. The apparatus of claim 29 wherein said securing mechanism comprises at least one expandable prong.

34. The apparatus of claim 29 wherein said securing mechanism comprises at least one lateral projection.

35. The apparatus of claim 20 wherein said pledget further comprises a hemostatic agent to chemically activate a clotting cascade.

36. The apparatus of claim 20 wherein said pusher bottom is initially positioned below said bleed back port and adjacent to said second end of said pledget.

37. The apparatus of claim 20 wherein said pusher bottom has a diameter less than or equal to said cannula inner diameter.

38. The apparatus of claim 20 wherein said pusher further comprises an extension between said top and said bottom wherein said extension has a small diameter to

maximize space within said cannula lumen to maximize a flow of blood out of said bleed back exit port.

39. The apparatus of claim 20 wherein said pusher bottom is initially positioned above said bleed back port to maximize space within said cannula lumen to maximize a flow of blood out of said bleed back exit port.

40. A method for facilitating hemostasis at a blood vessel puncture site, comprising:

advancing a cannula into a blood vessel lumen, said cannula having a bleed back port at a distal end, a pledget having a first end and a second end, said pledget second end positioned below said bleed back port, and a pusher having a top and a bottom, said pusher bottom slidably received in a cannula lumen at a cannula proximal end;

withdrawing said cannula, said pledget, said bleed back port, and said pusher simultaneously until a blood flow no longer exists a bleed back exit port;

holding said pusher at a fixed position;

pulling said cannula proximal end toward said top of said pusher; and

withdrawing said cannula and said pusher out of a tissue tract.

41. The method of claim 40 wherein said advancing further comprises inserting said cannula through a procedural sheath.

42. The method of claim 40 wherein said advancing further comprises inserting said cannula over a guidewire.

43. The method of claim 40 wherein said pusher further comprises a lumen extending between said top and said bottom.

44. The method of claim 43 wherein said bleed back exit port is located near said top.

45. The method of claim 40 wherein said pusher bottom has a diameter equal to or less than an inner diameter of said cannula.

46. The method of claim 40 wherein said bleed back port is located at said cannula proximal end.

47. The method of claim 40 further comprising:

measuring a first distance between said proximal end and said top;

measuring a second distance between said bleed back port and said bottom;

measuring a third distance between said distal end and said bleed back port; and

measuring a fourth distance between said first end and said second end.

48. The method of claim 47 wherein said third distance is greater than or equal to said fourth distance and said first distance is greater than or equal to a combination of said second and said third distance.

49. The method of claim 48 wherein said fourth distance is greater than said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent to said pusher top, said pledget first end is positioned within a wall of said blood vessel.

50. The method of claim 48 wherein said fourth distance is less than said second distance such that when said pusher is in a fixed position and said cannula proximal end is pulled adjacent said pusher top, said pledget first end is positioned within a lumen of said blood vessel.

51. The method of claim 48 wherein said fourth distance is equal to said second distance such that when said pusher is in a fixed position and said cannula proximal end

is pulled adjacent to said pusher top, said pledget first end is positioned adjacent said blood vessel puncture site.

52. The method of claim 40 wherein said advancing further comprising positioning said bottom above said bleed back exit port.

53. The method of claim 52 wherein said holding further comprises repositioning said bottom at said second distance.

54. The method of claim 40 wherein said pusher further comprises an extension between said top and said bottom wherein said extension has a small diameter to maximize space within said lumen of said cannula to maximize said blood flow out of said bleed back exit port.

55. The method of claim 54 wherein said advancing further comprises positioning said bottom of said pusher below said bleed back port.

56. The method of claim 55 wherein said holding further comprises repositioning said bottom at said second distance.

57. The method of claim 40 wherein said pledget first end has a diameter substantially equal to the inner diameter of said cannula.

58. The method of claim 40 wherein said pledget further comprises a hemostatic agent to chemically active a clotting cascade.

59. The apparatus of claim 40 wherein said pledget further comprises a securing mechanism.

60. The apparatus of claim 59 wherein said securing mechanism is a bioadhesive agent.

61. The apparatus of claim 59 wherein said securing mechanism is coupled to said pledget first end.

62. The apparatus of claim 59 wherein said securing mechanism is coupled to said pledget second end.

63. The apparatus of claim 59 wherein said securing mechanism comprises at least one expandable prong.

64. The apparatus of claim 59 wherein said securing mechanism comprises at least one lateral projection.

65. The apparatus of claim 59 wherein said securing mechanism is expandable.

66. The apparatus of claim 59 wherein said securing mechanism is absorbable.

67. A method for facilitating hemostasis at a arteriotomy of a blood vessel further comprising:

positioning a first end of a pledget at a distal end of a cannula below a bleed back port, said bleed back port located adjacent said distal end of said cannula, wherein the distance between said first end of the pledget and said bleed back port is greater than a length of said pledget;

inserting a pusher into a lumen of said cannula, said pusher having a bottom and a top;

positioning said bottom above said bleed back port a distance P, wherein said distance P is equal to the distance of said length of said pledget;

advancing said cannula, said pledget, said bleed back port, and said pusher simultaneously into a lumen of said blood vessel;

withdrawing said cannula, said pledget, said bleed back port, and said pusher simultaneously until a blood flow no longer exists a bleed back exit port;

holding said pusher at a fixed position; and

pulling a proximal end of said cannula adjacent said top of said pusher.

68. The method of claim 67 wherein said pulling further comprises retracting said cannula a distance greater than the combination of the distance P and the distance between the first end of the pledget and said bleed back port.

69. A method for facilitating hemostasis within the lumen of a blood vessel further comprising:

positioning a first end of a pledget at a distal end of a cannula below a bleed back port, said bleed back port located adjacent said distal end of said cannula, wherein the distance between said first end of the pledget and said bleed back port is greater than a length of said pledget;

inserting a pusher into a lumen of said cannula, said pusher having a bottom and a top;

positioning said bottom above said bleed back port a distance P, wherein said distance P is less than said length of said pledget;

advancing said cannula, said pledget, said bleed back port, and said pusher simultaneously into a lumen of said blood vessel;

withdrawing said cannula, said pledget, said bleed back port, and said pusher simultaneously until a blood flow no longer exists a bleed back exit port;

holding said pusher at a fixed position; and

pulling a proximal end of said cannula adjacent said top of said pusher.

70. The method of claim 69 wherein said pulling further comprises retracting said cannula a distance greater than or equal to the combination of the distance P and the distance between the first end of the pledget and said bleed back port.

71. A method for positioning a pledget adjacent a blood vessel puncture site further comprising:

positioning a first end of a pledget at a distal end of a cannula below a bleed back port, said bleed back port located adjacent said distal end of said cannula, wherein the distance between said first end of the pledget and said bleed back port is greater than a length of said pledget;

inserting a pusher into a lumen of said cannula, said pusher having a bottom and a top;

positioning said bottom above said bleed back port a distance P, wherein said distance P is greater than said length of the pledget;

advancing said cannula, said pledget, said bleed back port, and said pusher simultaneously into a lumen of said blood vessel;

withdrawing said cannula, said pledget, said bleed back port, and said pusher simultaneously until a blood flow no longer exists a bleed back exit port;

holding said pusher at a fixed position; and

pulling a proximal end of said cannula adjacent said top of said pusher.

72. The method of claim 71 wherein said pulling further comprises retracting said cannula a distance greater than or equal to the combination of the distance P and the distance between the first end of the pledget and said bleed back port.

73. A method for locating a hemostatic pledget at a blood vessel puncture site, comprising:

advancing a cannula into a tissue tract and into lumen of a blood vessel, said cannula having a bleed back port at a distal end, a pledget having a first end and a second end, said pledget second end positioned below said bleed back port, and a pusher having a top and a bottom, said pusher bottom slidably received in a lumen of said cannula at a distal end;

withdrawing said cannula, said pledget, said bleed back port, and said pusher simultaneously until a blood flow no longer exists a bleed back exit port;

advancing said pusher a distance R; and

withdrawing said cannula and said pusher simultaneously out of said tissue tract.

74. The method of claim 73 further comprises securing said pledget within said lumen of said blood vessel.

75. The apparatus of claim 74 wherein said securing further comprises a bioadhesive agent.

76. The apparatus of claim 74 wherein said securing further comprises at least one expandable prong.

77. The method of claim 76 wherein said distance R is equal to or greater than a length of said at least one expandable prong.

78. The method of claim 76 wherein said at least one expandable prong is absorbable.

79. The method of claim 74 wherein said securing comprises at least one lateral projection.

80. The method of claim 79 wherein said distance R is a length of said at least one lateral projection

81. The method of claim 79 wherein said at least one lateral projection is absorbable.

ABSTRACT OF THE DISCLOSURE

The present invention provides for a method and apparatus to facilitate hemostasis at a blood vessel puncture site having a cannula with a distal end, a proximal end, an inner diameter, and a lumen extending between said distal end and said proximal end; a bleed back port located near the distal end; a pusher having a top, a bottom, and a lumen extending between the top and bottom, the bottom is slidably received into the cannula lumen; a bleed back exit port located near the top; and a pledget having a first end and a second end, the first end positioned at the distal end within the cannula lumen, and the second end positioned below the bleed back port.

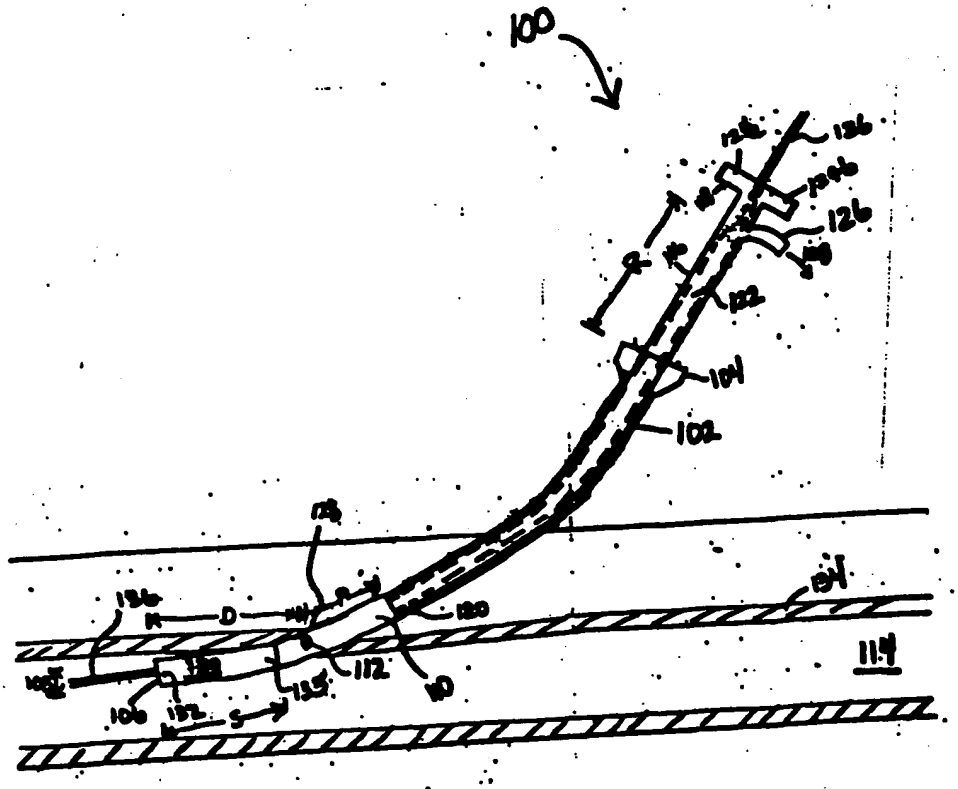


FIG. 1

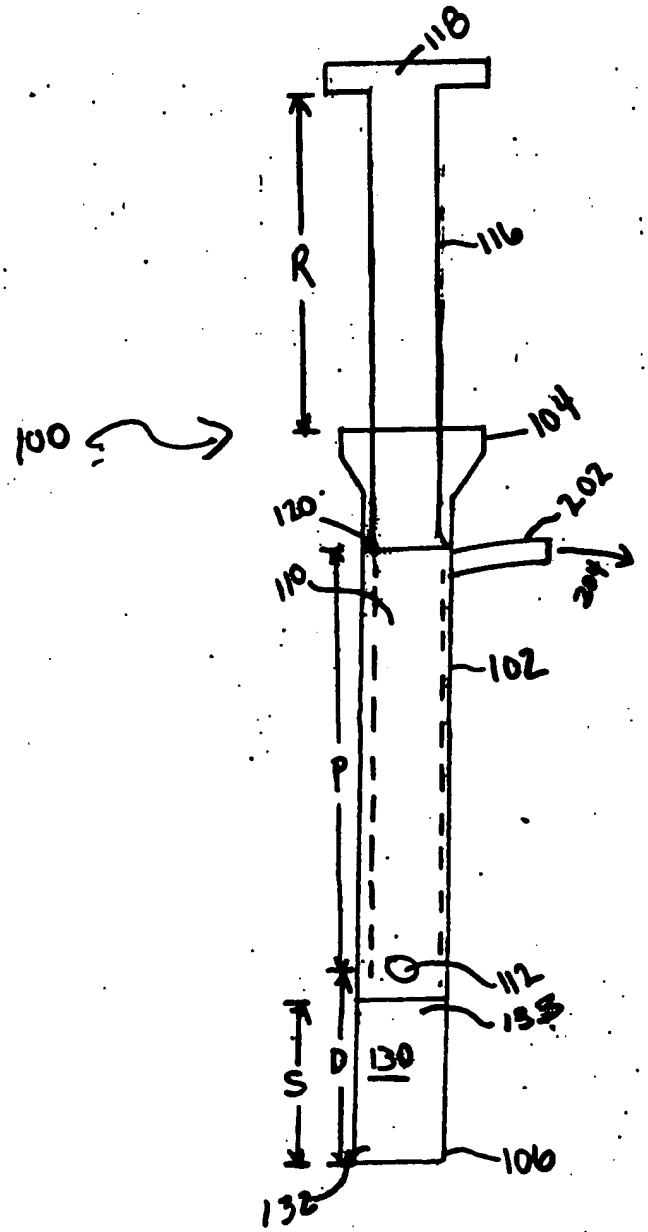


FIG. 2

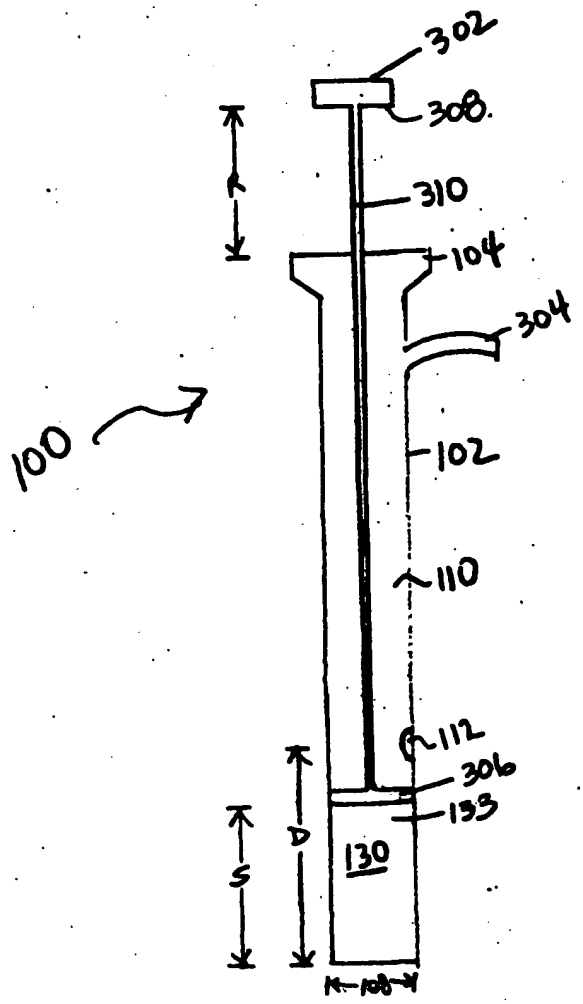


FIG. 3A

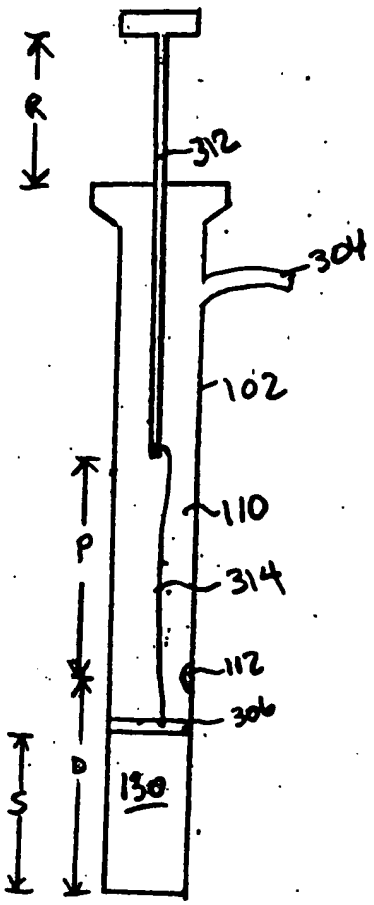


FIG. 3B

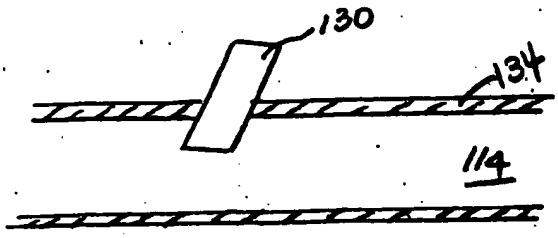


FIG. 4A

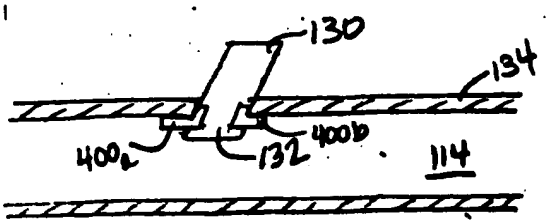


FIG. 4B

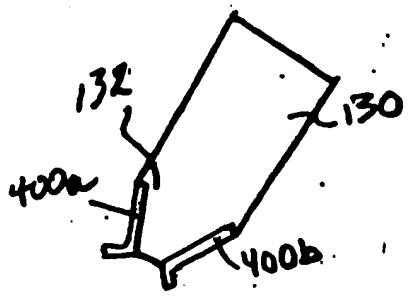


FIG. 4C

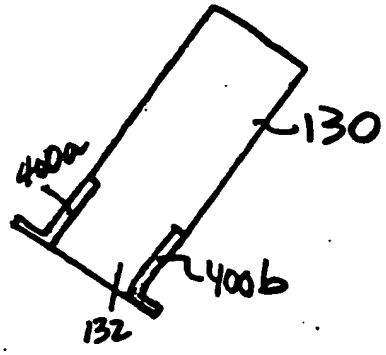


FIG. 4D

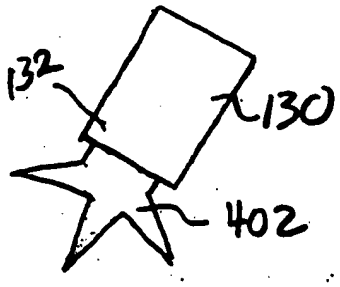


FIG. 4E

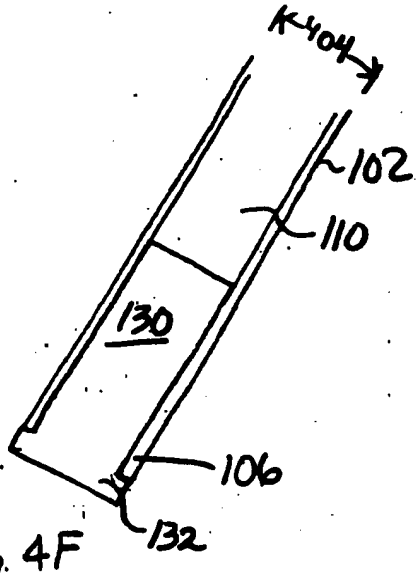


FIG. 4F

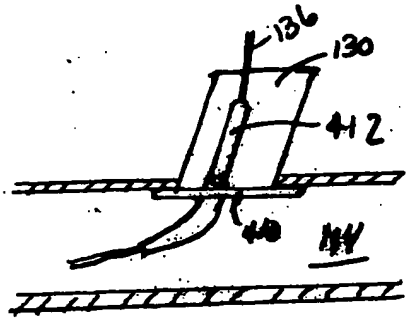


FIG. 4G

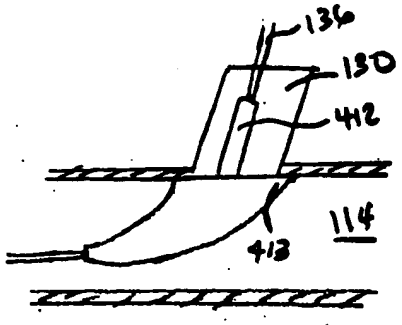


FIG 4H

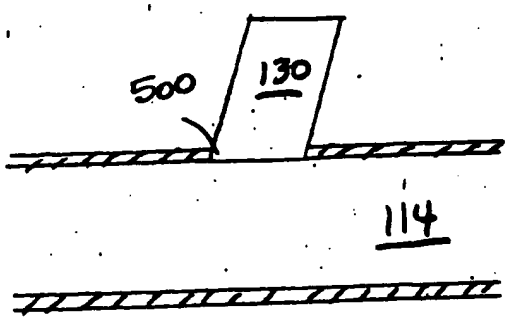


FIG. 5A

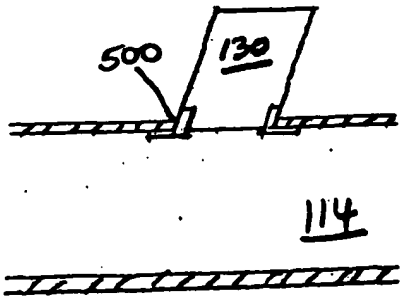


FIG. 5B

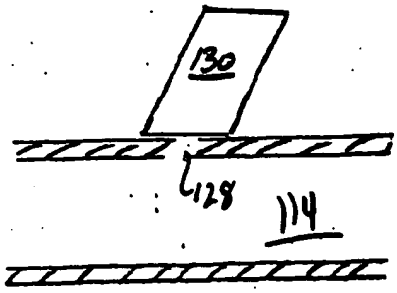


FIG. 6A

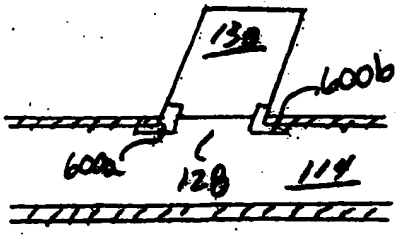


FIG. 6B

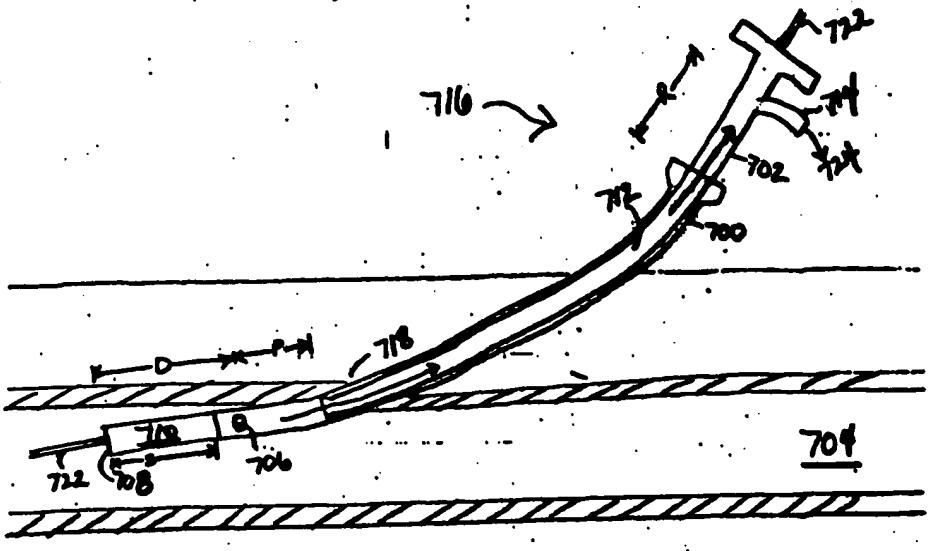


FIG. 7A

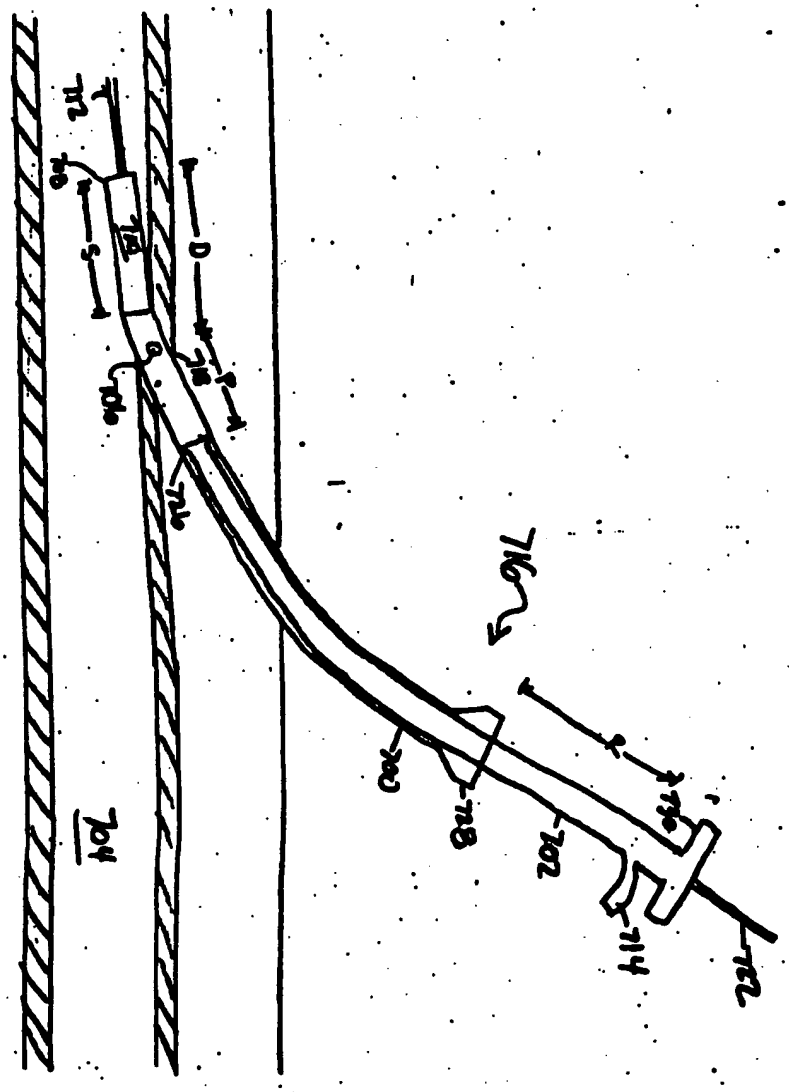


FIG. 7B

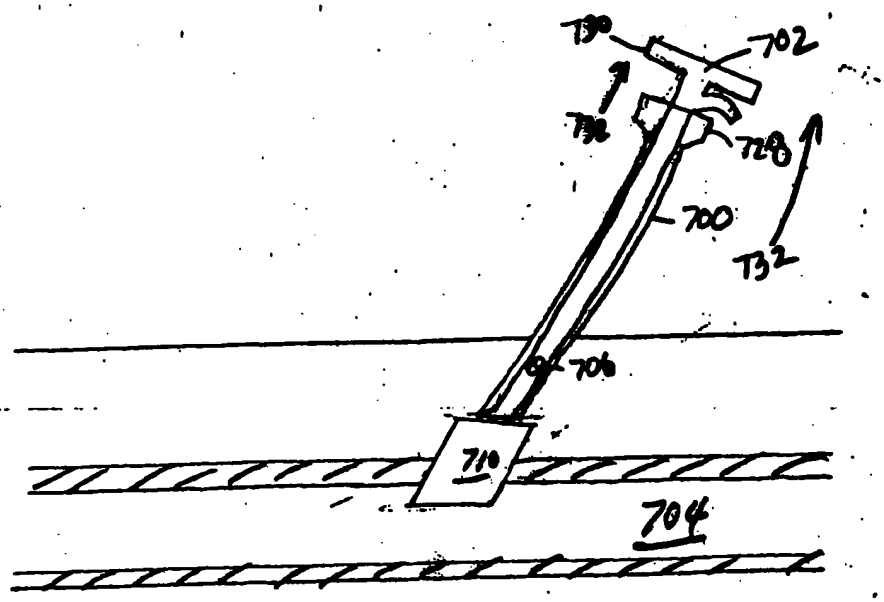


FIG. 7C

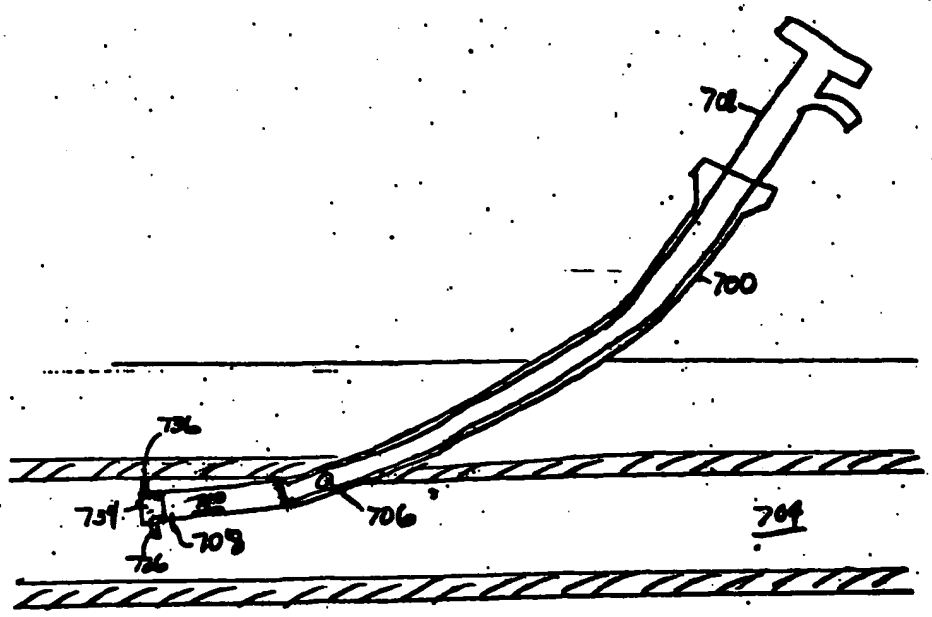


FIG. 7D

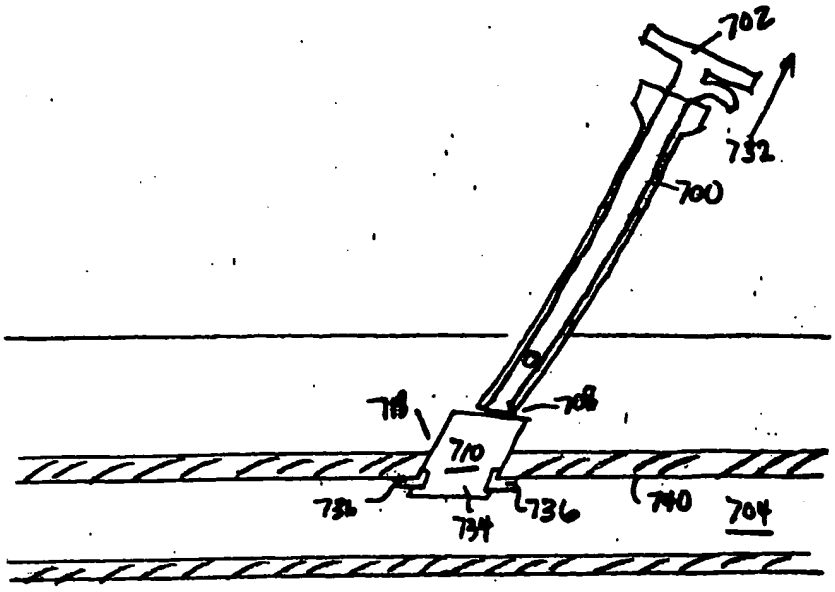

702
732
700
718
708
710
736
734
740
704

FIG. 7E

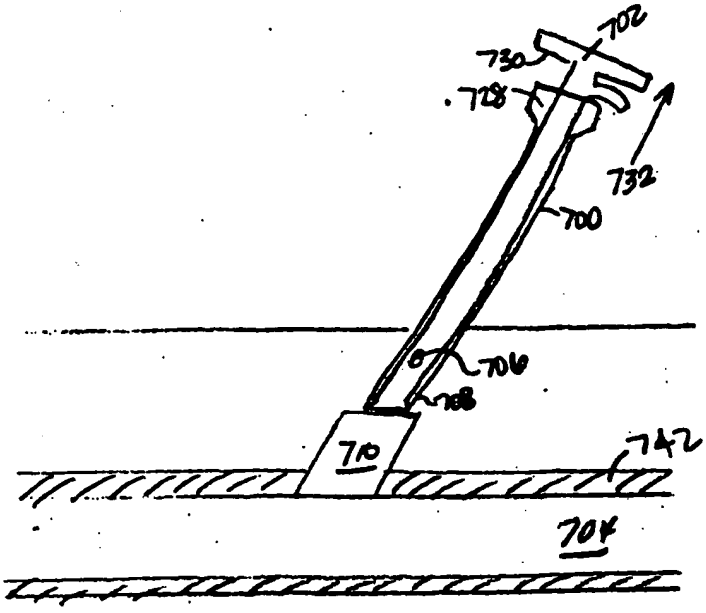

702
730
728
732
700
706
708
710
742
704

FIG. 7F

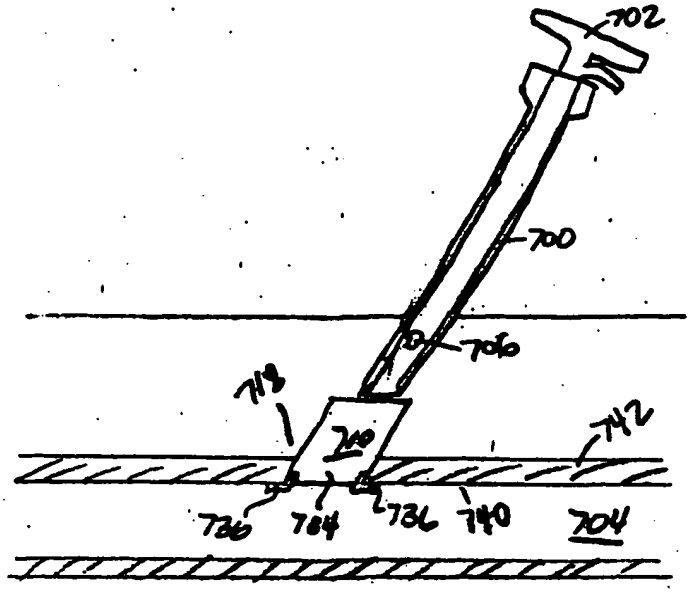

702
700
706
718
710
712
726
724
736
740
704

FIG. 7G

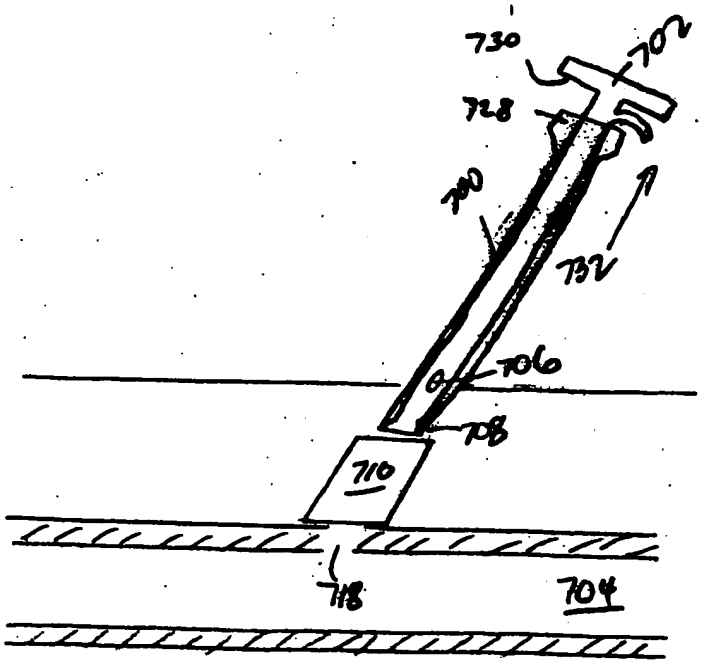

730
702
728
700
732
706
708
710
718
704

FIG. 7H.

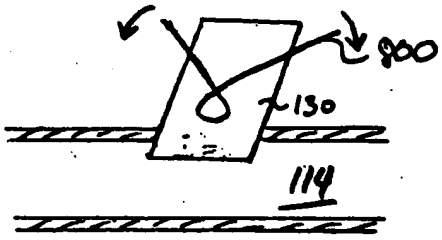


FIG. 8A

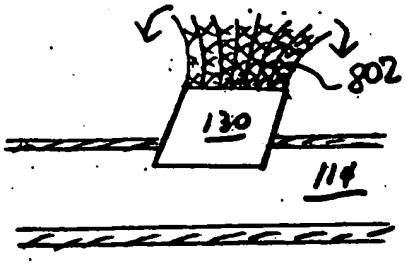


FIG. 8B

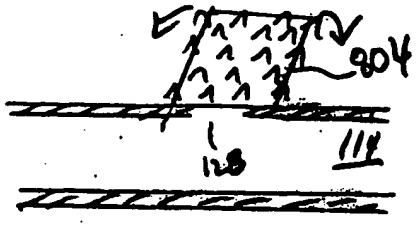


FIG. 8C

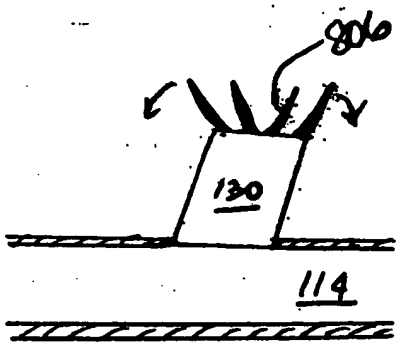


FIG. 8D